

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

k113830

B. Purpose for Submission:

New device

C. Measurand:

LDL-P (low density lipoprotein particle number), HDL cholesterol (HDL-C), and triglycerides

D. Type of Test:

Nuclear Magnetic Resonance (NMR) spectroscopy assay

E. Applicant:

LipoScience Inc.

F. Proprietary and Established Names:

NMR LipoProfile® test on Vantera® Clinical Analyzer

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
NSU	Class II	21 CFR 862.2570, Instrumentation for clinical multiplex test system	Clinical Chemistry (75)
MRR	Class I, meets limitations per 21 CFR 862.9(c)(4)	21 CFR 862.1475, Lipoprotein test system	Clinical Chemistry (75)
LBS		21 CFR 862.1175, Cholesterol test system	Clinical Chemistry (75)
CDT		21 CFR 862.1705, Triglyceride test system	Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

The Vantera® Clinical Analyzer is an automated laboratory test analyzer which measures the 400 MHz proton nuclear magnetic resonance (NMR) spectrum of clinical samples to produce signal amplitudes, converting these signal amplitudes to analyte concentration. The device includes a 400 MHz NMR spectrometer and software to analyze digitized spectral data. This instrumentation is intended to be used with NMR based assays to detect multiple analytes from clinical samples.

The *NMR LipoProfile*® test, when used with the Vantera® Clinical Analyzer, an automated NMR spectrometer, measures lipoprotein particles to quantify LDL particle number (LDL-P), HDL cholesterol (HDL-C), and triglycerides in human serum and plasma using nuclear magnetic resonance (NMR) spectroscopy. LDL-P and these NMR-derived concentrations of HDL-C and triglycerides are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease.

3. Special conditions for use statement(s):

For *in vitro* diagnostic use only, for prescription use only.

4. Special instrument requirements:

All performance was evaluated on the The Vantera® Clinical Analyzer

I. Device Description:

The test system includes the following components:

- **Diluent 1**(*NMR LipoProfile*® test) – 8 x 250mL bottles of aqueous solution containing Na₂EDTA (5.0mM), CaCl₂ (1.0mM), KCL (120mM), Na₂HPO₄ -7H₂O(50mM), pH 7.4, 6.0 M NaOH, 1.0 M HCl.

- **WASH** (NMR Fluidics System Solution) – single 2L bottle of Triton X-100-0.1%v/v, Liqui Nox 0.1% v/v in Type 2 water, pH 10.0, sodium bicarbonate (anhydrous), sodium carbonate (anhydrous), 6.0 M NaOH.

- **NMR Reference Standard (calibrator)** – 6 x 30mL bottles of 0.2% w/v aqueous solution of Trimethyl Acetate (TMA) disodium salt (15.0 mM) containing Na₂EDTA (5.0 mM), CaCl₂ (3.0 mM), KCl (120 nM), D₂O 10% v/v, 6.0 M NaOH, 1.0 M HCl. Each box of NMR

Reference Standard is supplied with specimen tube barcodes.

- **QC Material** – 2 levels of human based control material (6 x 3mL each) which include values for LDL-P, TG, and HDL-C as assigned at LipoScience.

The control materials contain human source material. Each donor unit is tested by FDA – approved methods and found non-reactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis C, and antibody to HIV-1/2.

All products using human source material should be handled as potentially infectious, because no test method can offer complete assurance that infectious agents are absent.

- **Vantera Clinical Analyzer** - 400 MHz proton nuclear magnetic resonance spectrometer interfaced with sample handling assembly, deconvolution software and provided with a system User’s Manual.

J. Substantial Equivalence Information:

1. Predicate device name(s):
 1. NMR Profiler and *NMR Lipoprofile* test
 2. Luminex LX 100/200 Instrument
2. Predicate 510(k) number(s):
 1. k111516
 2. k073506
3. Comparison with predicate:

Instruments:

Items	Vantera [®] Clinical Analyzer for use with <i>NMR LipoProfile</i> [®] test (Candidate Device)	Luminex LX 100/200 Instrument (Predicate Device) k073506
Similarities		
Instrument Intended Use	Same	A clinical multiplex instrument intended to measure and sort multiple signals generated in an <i>In Vitro</i> diagnostic assay from a clinical sample. This instrumentation is used with a specific assay to measure multiple similar analytes that establish a single indicator to aid in diagnosis. The device

		includes a signal reader unit, raw data storage mechanisms, data acquisition software and software to process detected signals.
Multi-Analyte	Same	Yes
System Fluidics	Same	Utilizes system fluidics to deliver sample to the site of sample analysis
System Calibration	Same	Calibration Required
Specimen Identification	Same	Barcode reader entry of sample ID
Data Acquisition Software	Same	Data acquisition software and software to process detected signals
Differences		
Test Principle	Nuclear magnetic resonance – 400 MHz proton NMR	Bead based multiplexing - Fluorescence
Sample handling	Serum/Plasma Samples are diluted onboard system	Samples are manually prepared then presented to system.

Device:

Items	Vantera [®] Clinical Analyzer for use with <i>NMR LipoProfile[®]</i> test (Candidate Device)	<i>LipoScience NMR LipoProfile[®]</i> test and NMR Profiler (Predicate Device) k111516
Similarities		
Device Intended Use	Same	For the measurement of lipoprotein particles to quantify LDL particle number (LDL-P), HDL cholesterol (HDL-C), and triglycerides in human serum and plasma using nuclear magnetic resonance (NMR) spectroscopy. LDL-P and these NMR-derived concentrations of HDL-C and triglycerides are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease

Test Principle	Same	Nuclear magnetic resonance – 400 MHz proton NMR
Multi-Analyte	Same	Yes
System Fluidics	Same	Manual
Sample Type	Same	Human Serum and Plasma
System Calibration	Same	Calibration Required
Specimen Identification	Same	Barcode reader entry of sample ID
Data Acquisition Software	Same	Data acquisition software and software to process detected signals
Spectral Deconvolution	Same	Linear least-squares with singular value decomposition of the spectra from each specimen.
Measuring Range LDL-P	Same	300-3500 nmol/L
Measuring Range TG	Same	5-1100 mg/dL
Measuring Range HDL-C	Same	7-140 mg/dL
Differences		
Sample handling	Serum/Plasma Samples are diluted onboard system	Samples are manually prepared then presented to system.
System Fluidics	Utilizes system fluidics to deliver sample to the site of sample analysis	Manual

K. Standard/Guidance Document Referenced (if applicable):

- CLSI Guideline EP05-A2: Evaluation of Precision Performance of Qualitative Measurement Methods
- CLSI Guideline EP06-A: Evaluation of the Linearity of Qualitative Measurement Methods
- CLSI Guideline EP07-A2: Interference Testing in Clinical Chemistry
- CLSI Guideline EP09-A2: Method Comparison and Bias Estimation Using Patient Samples
- CLSI Guideline EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation
- CLSI Guideline EP14-A2: Evaluation of Matrix Effects
- CLSI Guideline C28-A3: Defining Establishing, and Verifying Reference Intervals in the Clinical Laboratory
- IEC 610 I 0-1:200 I, 2nd Edition; Safety requirements for electrical equipment for measurement, control and laboratory use. Part I

L. Test Principle:

Vantera Clinical Analyzer

The Vantera Clinical Analyzer is a clinical laboratory analyzer that employs nuclear magnetic resonance spectroscopic detection to quantify multiple analytes in biological fluid specimens, specifically blood plasma and serum.

The Vantera Clinical Analyzer system design is divided into 3 major subassemblies: a sample handling assembly, an NMR subassembly, and an enclosure. The Vantera Clinical Analyzer control system is distributed across three separate computers:

- The Host (1U) controls user interface, data handling, results calculation, system startup and shutdown.
- The Process Control (4U) schedules and manages all activities required to process a sample, controls all hardware in the sample handling subsystem, and manages remote access to the system.
- The NMR Control Computer controls all magnet operations.

Two of these computers are contained within the Sample Handling Subassembly (1U and 4U) and one in the NMR Subassembly (NMR Console).

NMR LipoProfile test

The *NMR LipoProfile* test involves measurement of the 400 MHz proton NMR spectrum of a plasma/serum sample, deconvolution of the composite signal at approximately 0.8 ppm to produce signal amplitudes of the lipoprotein subclasses that contribute to the composite plasma/serum signal, and conversion of these subclass signal amplitudes to lipoprotein subclass concentrations. The ~0.8 ppm plasma NMR signal arises from the methyl group protons of the lipids carried in the LDL, HDL and VLDL subclasses of varying diameters. The NMR signals from the various lipoprotein subclasses have unique and distinctive frequencies and line shapes, each of which is accounted for in the deconvolution analysis model. Each subclass signal amplitude is proportional to the number of subclass particles emitting the signal, which enables subclass particle concentrations to be calculated from the subclass signal amplitudes derived from the spectral deconvolution analysis. LDL subclass particle concentrations, in units of nanomoles of particles per liter (nmol/L), are summed to give the reported total LDL particle concentration (LDL-P). By employing conversion factors assuming that the various lipoprotein subclass particles have cholesterol and triglyceride contents characteristic of normolipidemic individuals, HDL cholesterol and triglyceride concentrations are also derived.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within-run and within-laboratory precision were evaluated in accordance with the methods defined in the CLSI Guideline EP5-A, “Evaluation of Precision Performance of Clinical Chemistry Devices.”

Three serum pools with different analyte concentrations were tested in multiple runs over multiple days. For the Within-Lab, multiple instruments, operators and reagent lots were incorporated into the testing and a variance component analysis was conducted to estimate the individual sources of the total system variability.

Within-run precision - A single run of 20 replicates for the low, medium and high pool was conducted on one NMR instrument. A single operator conducted all three runs.

	Pool #1			Pool #2			Pool #3		
	Mean	SD	%CV	Mean	SD	%CV	Mean	SD	%CV
LDL-P, nmol/L	842.6	48.5	5.8	1309.5	39.1	3.0	1837.7	50.3	2.7
HDL-C, mg/dL	29.1	1.17	4.0	51.1	1.43	2.8	86.9	2.29	2.6
Triglycerides, mg/dL	70.1	1.6	2.3	169.2	3.5	2.1	356.1	4.2	1.2

Within-laboratory precision – Two runs per day with two replicates per run for three pools were tested on three instruments for a total of 20 testing days.

	Pool #1			Pool #2			Pool #3		
	Mean	SD	%CV	Mean	SD	%CV	Mean	SD	%CV
LDL-P, nmol/L	988.6	48.84	5.3	1266.7	32.57	4.0	1943.5	63.42	3.9
HDL-C, mg/dL	28.9	0.80	2.8	50.7	1.02	2.0	85.2	1.51	1.8
Triglycerides mg/dL	68.8	1.59	2.3	166.3	3.92	2.4	352.2	9.36	2.7

Reproducibility – A reproducibility study was conducted in accordance to EP5-A2 at 3 sites incorporating five levels of serum panels at or around the medical decision limits. The panels were tested for 5 days, 6 runs per day, 2 replicates per run. The overall precision estimates are described below.

	Pool #1			Pool #2			Pool #3		
	Mean	SD	%CV	Mean	SD	%CV	Mean	SD	%CV
LDL-P, nmol/L	520.2	52.94	10.2	1182.1	82.19	7.0	1343.4	97.37	7.2
HDL-C, mg/dL	20.1	1.26	6.3	30.3	2.60	8.6	52.0	2.45	4.7
Triglycerides, mg/dL	67.6	2.76	4.1	71.8	3.21	4.5	136.4	5.41	4.0

	Pool #4			Pool #5		
	Mean	SD	%CV	Mean	SD	%CV
LDL-P, nmol/L	1996.2	96.39	4.8	3214.8	165.44	5.1
HDL-C, mg/dL	75.8	4.56	6.0	88.2	3.91	4.4
Triglycerides, mg/dL	161.4	8.66	5.4	348.0	14.99	4.3

b. Linearity/assay reportable range:

Three serum pools were prepared from patient specimens with low, medium and high values of LDL-P, HDL-C and Triglycerides (TG) as determined by *NMR LipoProfile* test. The pools were mixed in different proportions to produce eleven (for LDL-P) or Twelve (12) (TG and HDL-C) different samples with widely varying target concentrations. Mean values from analysis of four replicates of each pool were compared to the expected target values to determine the percent bias for each sample. The serum pools were analyzed according to EP6-A. Tables and regression plots of the linearity data for LDL-P, HDL-P and Triglycerides are given below:

LDL-P Linear Regression Analysis:

$$y = 1.0193x + 7.8226$$

$$R^2 = 0.9949$$

Sample range tested: 248.8 – 4442.8

HDL-C Linear Regression Analysis:

$$y = 1.0486x - 0.3459$$

$$R^2 = 0.9961$$

Sample range tested: 5.0 – 151.5

TG Linear Regression Analysis:

$$y = 1.008x - 0.3979$$

$$R^2 = 0.9999$$

Sample range tested: 5.5 – 1356.3

Claimed Reportable Range for each analyte:

LDL-P	300 – 3500 nmol/L
HDL-C	7 – 140 mg/dL
TG	5 – 1100 mg/dL

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

The sponsor states in the labeling that this device has not been certified or tested by the Cholesterol Reference Method Laboratory Network.

Traceability for calibrator – TMA (Trimethylacetic acid, Sodium salt, from Trimethyl acetate hydrate CAS-No 143174-36-1, and Ethylenediamine Tetraacetic acid CAS-No 139-33-3) is used as the NMR calibrator for the NMR clinical analyzers. TMA is used routinely as a calibrator once daily during instrument startup to establish daily normalization factors. It also serves as a quality assessment tool to ensure quality NMR spectra are produced by the NMR analyzer. New calibrator material is run in parallel with the existing calibrator in five separate runs. The TMA calibrator is characterized by the manufacturer using infrared spectrum (chemical structure), elemental analysis, and titration.

Traceability for control – Controls are included with the *NMR LipoProfile*® test. Bio-Rad Liquichek controls (k012513) are obtained by LipoScience and are assigned target values and expiration dates in house by LipoScience prior to providing the control sets to the users. The LDL-P specific value assignment occurs via in-house created master calibrators which are traceable to a purchased source material characterized by lipoprotein metabolism profiling using a combination of electrophoresis, ultracentrifugation, and automated enzymatic quantification of cholesterol and triglycerides (fractions HDL, LDL, VLDL, and Lp[a]). Each lot of control set is value assigned from the master calibrators through evaluation of 5 replicate measurements per run using 3 instruments analyzing 2 runs per day for 2 days.

Stability – The stability protocol of the TMA calibrator material and the control sets was reviewed and found to be adequate. Stability studies support a stability claim of TMA calibrator stability for 18 months either refrigerated or at room temperature. Stability for the quality controls is designated by the manufacturer and confirmed using stability studies in house. The stability protocols and acceptance criteria were reviewed and found to be adequate, with a specific stability claim for LDL-P of 6 months frozen at -20°C

Sample Stability – The sample stability protocol and acceptance criteria were reviewed and found to be adequate. The stability study supports a claim of the following:

Tube	Processing	Storage	LDL-P Stability	TG Stability	HDL-C Stability
LipoTube (serum)	Normal	Refrigerated	8 days	12 days	7 days
	Delayed Centrifugation	Refrigerated	3 days	12 days	4 days
EDTA (plasma)	Normal	Refrigerated	12 days	12 days	8 days

d. *Detection limit:*

Limit of the Blank – Five delipidated serum pools containing very low concentration were tested in replicates of 4 for 3 days. The Limit of Blank (LoB) was calculated non-parametrically for each analyte and determined to be the following:

LDL-P: 0.0 nmol/L

HDL-C: 2.7 mg/dL

TG: 1.1 mg/dL

Limit of Detection – Non-lipoprotein specimens were analyzed 60 consecutive times for 3 days. The Limit of Detection (LoD) was calculated parametrically for each analyte and supported the claimed measuring range of the assay.

LDL-P: 40.7 nmol/L

HDL-C: 3.5 mg/dL

TG: 2.5 mg/dL

Limit of Quantitation – Five serum pools containing very low concentrations were tested in replicates of 4 for 3 days. The Limit of Quantification (LoQ) was mathematically calculated for each analyte by plotting the %CV on the Y-axis against low concentration pools and determined to be the following:

LDL-P: 132 nmol/L

HDL-C: 4.0 mg/dL

TG: 4.0 mg/dL

The LoQ values listed above support the sponsors claimed measuring ranges of:

LDL-P	300 – 3500 nmol/L
HDL-C	7 – 140 mg/dL
TG	5 – 1100 mg/dL

e. *Analytical specificity:*

Endogenous substances normally found in blood and exogenous substances (common and prescription drugs) were evaluated for potential interference with the *NMR LipoProfile*® test by LipoScience. Each potential interferent was diluted in the appropriate solvent and analyzed on the NMR Profiler to determine if it demonstrated

peak(s) in the 0.7 – 1.0 ppm region. Five endogenous agents and twenty three drugs were screened for potential interfering effects to NMR LipoProfile test using concentrations in accordance to CLSI EP7-A2 guidelines.

If a potentially interfering substance was suspected to have significant interference defined as difference from control greater than 10%, a spiking study was completed where the substance was added to sample pools containing two different levels of LDL-P, HDL-C and triglycerides for a paired difference test.

<i>Endogenous</i>		<i>Exogenous (OTC drugs, etc.)</i>			
<u>Potential Interferent</u>	<u>Test Concentration</u>	<u>Potential Interferent</u>	<u>Test Concentration</u>	<u>Potential Interferent</u>	<u>Test Concentration</u>
Hemoglobin	0.5 g/dL	Acetaminophen	1324 µmol/L	Metformin Hydrochloride	3.62 mmol/L
Bilirubin, unconj.	342 µmol/L 20 mg/dL	Acetylsalicylic acid	3.62 mmol/L	Metoprolol tartrate	18.7 µmol/L
Creatinine	442 µmol/L 5 mg/dL	Atorvastatin	600 µg Eq/L	Naproxen Sodium	2170 µmol/L
Urea	42.9 mmol/L 260 mg/dL	Clopidogrel hydrogensulfate**	95.7 µmol/L	Nicotinic Acid Sodium salt	8.28 mmol/L
Uric acid	1.4 mmol/L 23.5 mg/dL	Enalaprilat Dihydrate	0.86 µmol/L	Nifedipine	1156 nmol/L
Protein (albumin)	6 g/dL, 60g/L	Fenofibrate	125 µmol/L	Pioglitazone hydrochloride	152.7µmol/L
Bilirubin, conj	342 µmol/L 28.9 mg/dL	Furosemide	181 µmol/L	Piroxicam	181 µmol/L
		Glipizide	4.48 µmol/L	Pravastatin	107.5 µmol/L
		Hydralazine hydrochloride	915.4 µmol/L	Salicylic Acid*	1.3 mmol/L
		Heparin	3000U/L	Simvastatin	114.7 µmol/L

Ibuprofen Sodium salt 2425 µmol/L

Isosorbide dinitrate 636 nmol/L

Menhaden oil (Fish Oil) 2.4 mg/mL

*Salicylic acid at ≥ 1.3 mmol/L was determined to interfere with LDL-P

**Clopidogrel hydrogensulfate at ≥ 95.7 µmol/L was determined to interfere with LDL-P

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

LDL-P: The comparison was conducted in agreement with CLSI EP9-A2: *Method Comparison and Bias Estimation Using Patient Samples*. The study involved testing singlicates followed by statistical analysis of 1482 freshly-collected clinical de-identified specimens across the range of the LDL-P test on the Vantera Clinical Analyzer (candidate device) vs the NMR Profiler (predicate device). Bias was calculated for LDL-P from the linear regression line at the medical decision limits of 1000, 1300 and 1600 nmol/L as well. The range of the samples was 303 to 3479 nmol/L.

Linear regression/least squares analysis:

$$y = 1.03x - 36.60$$

$$r = 0.978$$

Observed LDL-P Bias per linear regression at Medical Decision Limits:

LDL-P (nmol/L)	Absolute Bias	Percent Bias (%)
1000	-10.0	-1.0
1300	-2.0	-0.2
1600	6.0	0.4

In addition to conducting a method comparison for the overall data set, the data were classified into the three following segments based on LDL-P values; (1) results below the medical decision limits of 1000 nmol/L, (2) results between 1000 and 1600 nmol/L and (3) results above 1600 nmol/L. For each segment the bias was determined. The determined % Bias for each segment was less than 5% for each level).

HDL-C: The comparison was conducted in agreement with CLSI EP9-A2: *Method Comparison and Bias Estimation Using Patient Samples*. The study involved testing singlicates followed by statistical analysis of 1518 freshly-collected clinical de-identified specimens across the range of the HDL-C test on the Vantera Clinical Analyzer (candidate device) vs the NMR Profiler (predicate device). Bias was calculated for HDL-C from the linear regression line at the medical decision limits of 40 and 60 mg/dL as well. The range of the samples was 7.0 to 132 mg/dL.

Linear regression/least squares analysis:

$$y = 1.04x - 1.20$$

$$r = 0.989$$

Observed HDL-C Bias per linear regression at Medical Decision Limits:

HDL-C (mg/dL)	Absolute Bias	Percent Bias (%)
40	0.3	0.8
60	1.1	1.8

In addition to conducting a method comparison for the overall data set, the data were classified into the three following segments based on HDL-C values; (1) results below the medical decision limits of 40 mg/dL, (2) results between 40 and 60 mg/dL and (3) results above 60 mg/dL. For each segment the bias was determined. The determined % Bias for each segment was less than 3% for each level.

TG: The comparison was conducted in agreement with CLSI EP9-A2: *Method Comparison and Bias Estimation Using Patient Samples*. The study involved testing singlicates followed by statistical analysis of 1520 freshly-collected clinical de-identified specimens across the range of the TG test on the Vantera Clinical Analyzer (candidate device) vs the NMR Profiler (predicate device). Bias was calculated for TG from the linear regression line at the medical decision limits of 150, 200 and 500 mg/dL as well. The range of the samples was 18.0 to 1095 mg/dL.

Linear regression/least squares analysis:

$$y = 1.00x + 0.92$$

$$r = 0.998$$

Observed TG Bias per linear regression at Medical Decision Limits:

TG (mg/dL)	Absolute Bias	Percent Bias (%)
150	1.2	0.8
200	1.3	0.7
500	1.8	0.4

In addition to conducting a method comparison for the overall data set, the data were classified into the three following segments based on TG values; (1) results below the medical decision limits of 150 mg/dL, (2) results between 150 and 200 mg/dL and (3) results above 200 mg/dL. For each segment the bias was determined. The determined % Bias for each segment was less than 3% for each level.

b. Matrix comparison:

Samples from 50 subjects (46 native and 4 contrived) were analyzed for each analyte by collecting the patient specimen into each of the claimed tube types. Comparative analysis of the LipoTube vs plain serum and EDTA plasma resulted in the following:

LipoTube vs Plain Serum

	LDL-P (nmol/L)	TG (mg/dL)	HDL-C (mg/dL)
Slope	0.9678	1.002	0.9739
Y-Int	26.4	-0.417	1.589
R sq	0.96	0.99	0.99

LipoTube vs EDTA Plasma

	LDL-P (nmol/L)	TG (mg/dL)	HDL-C (mg/dL)
Slope	0.9442	0.9212	0.9339
Y-Int	-13.9	2.414	2.079
R sq	0.97	1.00	0.99

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

See expected values below

5. Expected values/Reference range:

The sponsor conducted a reference range study in order to determine the normal distribution of LDL-P levels expected in a representative sampling of the general population. Healthy adult patient plasma samples were obtained (n=452) and analyzed (age ranging from 18 to 84 years). Samples or patients with specific history of diabetes or cardiac, renal or lipid disease were excluded, as well as any patients who were pregnant or being treated for cancer. Sample results were analyzed together, and also were partitioned into percentiles and separated based upon patient sex and age. The results of the reference range study are listed in the tables below:

Distribution of LDL-P Observed in a Reference Population

	All (n=452)	Men (n=158)	Women (n=294)	All (n=452)	Men (n=158)	Women (n=294)
Percentile	LDL-P (nmol/L)	LDL-P (nmol/L)	LDL-P (nmol/L)	LDL-C (mg/dL)	LDL-C (mg/dL)	LDL-C (mg/dL)
5	539	528	542	63	62	65
10	643	713	638	75	76	75
20	784	883	749	84	90	83
30	909	1004	863	94	100	91
40	1009	1087	970	102	107	98
50	1127	1241	1070	109	113	109
60	1248	1366	1202	118	128	115
70	1396	1505	1322	129	137	124
80	1572	1676	1482	140	147	136
90	1894	1941	1818	157	161	151
95	2047	2169	1986	169	171	169

Distribution of LDL-P Observed in a Reference Population of Healthy Subjects Ages 18 - 44

	All (n=329)	Men (n=115)	Women (n=214)	All (n=329)	Men (n=115)	Women (n=214)
Percentile	LDL-P (nmol/L)	LDL-P (nmol/L)	LDL-P (nmol/L)	LDL-C (mg/dL)	LDL-C (mg/dL)	LDL-C (mg/dL)
5	532	513	528	62	61	64
10	634	654	630	72	72	72
20	753	862	726	82	89	81
30	885	961	820	90	99	87
40	966	1041	930	98	106	94
50	1045	1149	1008	107	110	101

60	1191	1322	1115	113	126	109
70	1328	1466	1251	122	135	118
80	1492	1639	1406	136	145	127
90	1807	1945	1666	150	161	146
95	2028	2241	1976	165	171	156

Distribution of LDL-P Observed in a Reference Population of Healthy Subjects \geq Age 45

	All (n=123)	Men (n=43)	Women (n=80)	All (n=123)	Men (n=43)	Women (n=80)
Percentile	LDL-P (nmol/L)	LDL-P (nmol/L)	LDL-P (nmol/L)	LDL-C (mg/dL)	LDL-C (mg/dL)	LDL-C (mg/dL)
5	590	559	586	71	56	71
10	733	772	726	83	78	84
20	871	951	842	94	93	94
30	1025	1186	998	106	103	109
40	1188	1290	1158	113	110	115
50	1295	1364	1224	123	119	124
60	1402	1478	1368	134	133	134
70	1545	1643	1504	140	141	140
80	1752	1731	1796	150	153	146
90	1949	1934	1949	164	162	169
95	2075	2562	2016	186	181	188

Labeling for expected values states that each laboratory should verify the validity of the stated reference range values for the population the laboratory serves.

HDL concentration and triglycerides: The proposed device has similar reference values as the predicate. The reference values for patient classification have been recommended by the NCEP and taken from literature* for HDL cholesterol and triglycerides for the assessment and management of CVD risk. The labeling states that each laboratory should verify the validity of these reference values for the population it serves.

HDL Cholesterol, mg/dL Classification		Triglycerides, mg/dL Classification			
<i>Low</i>	<i>High</i>	<i>Normal</i>	<i>Borderline High</i>	<i>High</i>	<i>Very High</i>
< 40	\geq 60	< 150	150 - 199	200 - 499	> 500

*Expert Panel on Detection, *Evaluation and Treatment of High Cholesterol in Adults (Adult Treatment Panel III)*, May (2001).

NIH Publication No. 01 3305, *ATP III Guidelines At-A-Glance*, Quick Desk Reference, May (2001).

NIH Publication No. 01 3670, *Third Report of National Cholesterol Education Program (NCEP)*

N. Instrument Name:

Vantera Clinical Analyzer

O. System Descriptions:

1. Modes of Operation:

Not applicable

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes ___X___ or No _____

3. Specimen Identification:

Internal barcode scanner identifies the specimens and automatically loads identification into the software.

4. Specimen Sampling and Handling:

Samples are loaded onto the instrument manually and samples are scanned and diluted / prepared automatically by the system.

5. Calibration:

Instrument calibration occurs daily (once every eight-hour shift) with the provided TMA calibrator (trimethyl acetic acid) to ensure the homogeneity of the magnetic field (line-shape specifications), to check the temperature of the NMR system, and to calculate the daily normalization factor. Calibration procedures are described in the labeling, and include a manual loading of the calibrant and automatic calibration by the instrument software.

6. Quality Control:

Quality controls are treated as specimens with specific control barcode labels that are provided with the system. The operator's manual recommends running the quality controls once daily or in accordance with the laboratory practice.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not applicable

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.